Claims

1. A pharmaceutical delivery system for oral delivery of the antioxidants vitamin C and vitamin E to obtain high concentrations thereof and a controlled ratio between vitamin C and vitamin E in blood plasma in humans or animals, c h a r a c t e r i z e d in that it has a slow release of vitamin C and a plain release of vitamin E.

2. A pharmaceutical delivery system according to claim 1, c h a r a c t e r i z e d in that it is a system comprising a tablet comprising at least two non-identical delivery principles , wherein

(A) one delivery principle comprises

(i) vitamin C;

(ii) a pharmaceutically acceptable excipient for controlling the slow release of vitamin C; and

(iii) other pharmaceutically acceptable excipients; and

(B) another delivery principle comprises

(i) vitamin E; and

(ii) pharmaceutically acceptable excipients.

3. A pharmaceutical delivery system according to claim 1 or 2, c h a r a c t e r i z e d in that the ratio between vitamin C and vitamin E in the blood plasma is from 1:1 to 3:1.

4. A pharmaceutical delivery system according to claim 3, c h a r a c t e r i z e d in that the ratio between vitamin C and vitamin E in the blood plasma is about 2.2:1.

5. A pharmaceutical delivery system according to any of the preceeding claims, c h a r a c t e r i z e d in that the concentration of vitamin E in human blood plasma is raised to at least 20 μmol/litre, preferably at least 30 μmol/litre, such as at least 40 or at least 50 μmol/litre , most preferably at least 55 μmol/litre and the concentration of vitamin C is raised to at least 40 μmol/litre, preferably at lease 60 μmol/litre, such as at least 70, 80 , 90 μmol/litre, most preferably at least 100 μmol/litre.

6. A pharmaceutical delivery system according to any of the preceding claims, c h a r a c t e r i z e d in that vitamin C is ascorbic acid and vitamin E is selected from the group

comprising d-α-tocopheryl acetate, d-α-tocopheryl acid succinate, d-α-tocopherol, d-β-tocopherol, d-γ-tocopherol, d-δ-tocopherol, d-α-tocotrienol, d-β-tocotrienol, d-γ-tocotrienol, d-δ-tocotrienol, dl-α-tocopherol, dl-α-tocopheryl acetate, dl-α-tocopheryl calcium succinate, dl-α-tocopheryl nicotinate, dl-α-tocopheryl linoleate/oleate and all other possible derivatives or stereo isomeric forms of the above compounds.

7. A pharmaceutical delivery system according to any of the preceding claims, c h a r a c t e r i z e d in that the system delivers a daily dose of each of the vitamins corresponding to 60 mg - 2 g of vitamin C and 10 mg - 800 mg of vitamin E.

8. A pharmaceutical delivery system according to claim 7, wherein the daily dose of vitamin C corresponds to 100 mg - 1.5 g of ascorbic acid, such as 200 mg - 1 g, most preferably corresponding to 250 mg -750 mg of ascorbic acid, preferably 300 mg -600 mg, particularly corresponding to 500 mg of ascorbic acid.

9. A pharmaceutical delivery system according to claim 7, wherein the daily dose of vitamin E corresponds to 50 mg - 500 mg of α-tocopherol, such as 100 mg - 250 mg, most preferably to 150 mg -200 mg of α-tocopherol, preferably 175 mg -190 mg, particularly corresponding to 180-185 mg of α-tocopherol, most preferably 182 mg.

10. A pharmaceutical delivery system according to claim 7, wherein the daily dose of vitamin C and E is delivered by at least one dosage unit, such as 1 to 8 dosage units, preferably at most 4 dosage units, such as at most 3 dosage units, preferably at most 2 dosage units, such as 2 or 1 dosage unit, particularly 2 dosage units.

11. A pharmaceutical delivery system according to claim 10, wherein the daily dose of vitamin C and E is delivered by 2 dosage units each dosage unit comprising i) from approximately 200 to 300 mg of vitamin C, such as 200, 225, 250, 275, or 300 mg, preferably 250 mg of vitamin C and ii) approximately 80 to 120 mg of vitamin E, such as from 80 to 100 mg preferably about 90 mg, such as 91 mg, 92, 93, 94, 95, 96, 97, 98, 99 mg of vitamin E, preferably 91 mg.

102 b/c of Test A

12. A pharmaceutical delivery system according to any of the preceding claims, c h a r a c t e r i z e d in that less than 40% of vitamin C is dissolved after 1 hour under the conditions of Test A, from 50 to 80% of vitamin C is dissolved after 3 hours under the

conditions of Test A, and more than 90% of vitamin C is dissolved after 7 hours under the conditions of Test A.

13. A pharmaceutical delivery system according to any of the preceding claims, c h a r a c t e r i z e d in that at least 90% of vitamin E is dissolved in less than 30 minutes under the conditions of Test B, such as in less than 15 minutes.

14. A pharmaceutical delivery system according to any of the preceding claims for preventing or treating conditions, diseases and disorders involving oxidative stress.

15. A pharmaceutical delivery system according to claim 14, wherein the conditions, diseases and disorders involving oxidative stress are selected from the group consisting of atherosclerosis, cancer, type I diabetes, type II diabetes, diabetic nephropathy, for skin damage, scar tissue, central nervous system disorders and degeneration, neural degeneration in general, such as for example in Alzheimer's Disease, for inflammation, fertility / fecundity diseases and disorders, conditions, diseases and disorders related to sun exposure, diseases and disorders related to ageing, for treatment and prevention of cataracts, for anticoagulation and nitrate-tolerance.

16. A pharmaceutical delivery system according to claim 15, wherein the conditions, diseases and disorders involving oxidative stress are selected from the group consisting of atherosclerosis, type I diabetes, type II diabetes, diabetic nephropathy, central nervous system disorders and degeneration, neural degeneration in general, such as for example in Alzheimer's Disease, conditions, diseases and disorders related to sun exposure, cataracts.

17. A method of treating or preventing oxidative stress disorders and associated diseases and conditions comprising the administration to an individual a combination of vitamin C and vitamin E in sufficient amounts so as to raise, the concentration of said vitamins in blood plasma sufficiently and to a ratio of from 1:1 to 3:1, preferably 2.2:1, in not more than 8 weeks from the first administration.

18. A method according to claim 19, wherein the raising is within 7 weeks of the first administration, such as within 6 weeks, preferably within 5 weeks, most preferably within 4 weeks.

19. A method according to any of claims 17 to 18, wherein the concentration of vitamin E is at least 20 μmol/litre, preferably at least 30 μmol/litre, such as at least 40 or at least 50 μmol/litre , most preferably at least 55 μmol/litre and the concentration of vitamin C is raised to at least 40 μmol/litre, preferably at lease 60 μmol/litre, such as at least 70, 80 , 90 μmol/litre, most preferably at least 100 μmol/litre.

20. A method according to any of claims 17 to 19, wherein the concentrations of vitamins C and E concomitantly present in the blood plasma are from about 102 to 142 μmol/litre of vitamin C and from about 46 to 65 μmol/litre of vitamin E, such as 112 μmol/litre of vitamin C and 51 μmol/litre of vitamin E, 122 μmol/litre of vitamin C and 55.5 μmol/litre of vitamin E, 132 μmol/litre of vitamin C and 60 μmol/litre of vitamin E, or 142 μmol/litre of vitamin C and 65 μmol/litre of vitamin E, especially preferred concentrations of the vitamins in human blood plasma are 132 μmol/litre of vitamin C and 60 μmol/litre of vitamin E.

21. A method according to any of claims 17 to 20, wherein the administration is of an at least once daily dose of dosage units comprising slow release formulation vitamin C and plain release vitamin E.

22. A method according to claim 21, wherein the slow release formulation releases less than 40% of vitamin C after 1 hour under the conditions of Test A, from 50 to 80% of vitamin C is released after 3 hours under the conditions of Test A, and more than 90% of vitamin C is dissolved after 7 hours under the conditions of Test A and the plain release formulation releases at least 90% of vitamin E is dissolved in less than 30 minutes under the conditions of Test B, such as in less than 15 minutes.

23. A method according to claim 21, wherein the daily dose of vitamin E corresponds to 50 mg - 500 mg of α-tocopherol, such as 100 mg - 250 mg, most preferably to 150 mg - 200 mg of α-tocopherol, preferably 175 mg -190 mg, particularly corresponding to 180-185 mg of α-tocopherol, most preferably 182 mg.

24. A method according to claim 21, wherein the daily dose of vitamin C corresponds to 100 mg - 1.5 g of ascorbic acid, such as 200 mg - 1 g, most preferably corresponding to

250 mg -750 mg of ascorbic acid, preferably 300 mg -600 mg, particularly corresponding to 500 mg of ascorbic acid

25. A method according to claim 21, wherein the at least once daily dose is of at most 8 dosage units, such as at most 6 dosage units, such as at most 5 dosage units, such as 4, 3, 2, or 1, preferably 2 or 1, most preferably 2.

26. A method according to claim 21, wherein the daily dose of vitamin C and E is delivered by 2 dosage units each dosage unit comprising i) from approximately 200 to 300 mg of vitamin C, such as 200, 225, 250, 275, or 300 mg, preferably 250 mg of vitamin C and ii) approximately 80 to 120 mg of vitamin E, such as from 80 to 100 mg preferably about 90 mg, such as 91 mg, 92, 93, 94, 95, 96, 97, 98, 99 mg of vitamin E, preferably 91 mg.

27. A method of treating or preventing oxidative stress disorders and associated diseases and conditions comprising the daily administration to an individual at least one dosage unit comprising a combination of vitamin C and vitamin E in sufficient amounts so as to raise the concentration of said vitamins in blood plasma sufficiently and to a controlled ratio wherein said vitamin C is formulated in a slow-release preparation and vitamin E is formulated in plain-release formulation.

28. A method according to claim 27, wherein the controlled ratio is from 1:1 to 3:1, preferably 2.2:1, of vitamin C to vitamin E, as measured within 8 weeks.

29. A method according to claim 28, wherein the concentration of vitamin E is at least 20 μmol/litre, preferably at least 30 μmol/litre, such as at least 40 or at least 50 μmol/litre , most preferably at least 55 μmol/litre and the concentration of vitamin C is raised to at least 40 μmol/litre, preferably at lease 60 μmol/litre, such as at least 70, 80 , 90 μmol/litre, most preferably at least 100 μmol/litre.

30. A method according to any of claims 27 to 29, wherein the concentrations of vitamins C and E concomitantly present in the blood plasma are from about 102 to 142 μmol/litre of vitamin C and from about 46 to 65 μmol/litre of vitamin E, such as 112 μmol/litre of vitamin C and 51 μmol/litre of vitamin E, 122 μmol/litre of vitamin C and 55.5 μmol/litre of vitamin E, 132 μmol/litre of vitamin C and 60 μmol/litre of vitamin E, or 142 μmol/litre of vitamin C

and 65 µmol/litre of vitamin E, especially preferred concentrations of the vitamins in human blood plasma are 132 µmol/litre of vitamin C and 60 µmol/litre of vitamin E.

31. A method according to claim 27, wherein the at least one dosage unit is at most 8 dosage units, such as at most 6 dosage units, such as at most 5 dosage units, such as 4, 3, 2, or 1, preferably 2 or 1, most preferably 2 dosage units.

32. A method according to claim 27, wherein the daily administration is of daily dose of vitamin E corresponding to 50 mg - 500 mg of α-tocopherol, such as 100 mg - 250 mg, most preferably to 150 mg -200 mg of α-tocopherol, preferably 175 mg -190 mg, particularly corresponding to 180-185 mg of α-tocopherol, most preferably 182 mg.

33. A method according to claim 27, wherein the daily administration is of daily dose of vitamin C corresponds to 100 mg - 1.5 g of ascorbic acid, such as 200 mg - 1 g, most preferably corresponding to 250 mg -750 mg of ascorbic acid, preferably 300 mg -600 mg, particularly corresponding to 500 mg of ascorbic acid.

34. Use of a combination of vitamin C and vitamin E for the preparation of a drug or drug system for treating or preventing atherosclerosis or other diseases or conditions responsive to antioxidants, wherein said vitamins are incorporated in the patients blood plasma in high concentrations and in a controlled ratio, c h a r a c t e r i z e d in that the drug has a slow release of vitamin C and a normal release of vitamin E.

35. Use according to claim 34, c h a r a c t e r i z e d in that the ratio between vitamin C and vitamin E in the blood plasma varies from 1:10 to 10:1, preferably from 1:5 to 5:1, and especially from 1:1 to 3:1.

36. Use according to claim 34, c h a r a c t e r i z e d in that the ratio between vitamin C and vitamin E in the blood plasma is about 2.2:1.

37. Use according to any of the claims 34 to 36, c h a r a c t e r i z e d in that the concentration of vitamin E in human blood plasma is raised to at least 20 µmol/litre, preferably at least 30 µmol/litre, such as at least 40 or at least 50 µmol/litre , most preferably at least 55 µmol/litre and the concentration of vitamin C is raised to at least 40

μmol/litre, preferably at lease 60 μmol/litre, such as at least 70, 80, 90 μmol/litre, most preferably at least 100 μmol/litre.